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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,888	07/17/2003	Robert Gurny	4-20437D	7666

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,888	GURNY ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6 and 32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6 and 32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The RCE dated 11-17-05 is acknowledged.

Claims included in the prosecution are 1, 4-6 and 32-37.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1, 4-6 and 32-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites 'active agent having low water solubility encapsulated in nanoparticles comprising solubilizing agent'. It is unclear what this solubilizer solubilizes.

It is unclear as to what applicant intends to convey by 'polyvinyl alcohol has a degree of hydrolysis greater than 70%' as recited in claim 33. What does an alcohol hydrolyze to? Instant specification does not explain this aspect.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that polyvinyl alcohol is produced by the hydrolysis of polyvinyl acetate and that the degree of hydrolysis of polyvinyl alcohol refers to varying levels of hydrolysis. This argument would have been persuasive if the compound recited is polyvinyl alcohol. However, instant claims recite polyvinyl alcohol and not polyvinyl

acetate. That means the entire molecule is polyvinyl alcohol and therefore there is no degree of hydrolysis (100 % hydrolyzed from polyvinyl acetate).

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1, 4-6 and 32-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allemann et al (international Journal of Pharmacology, 1992) of record by itself or in combination with Kawata (4,343,789) or Igari (5,482,706) or Kantor (4,895,725) by themselves or in combination.

> Allemann et al disclose a process of preparation of polymeric nanodispersions containing water soluble polymer (polyvinyl alcohol) and Eudragit S (anionic polymer which is soluble from pH 7 upwards (abstract and

page 248). What is lacking in Allemann is the teaching of the use of these nanospheres for encapsulating water insoluble drugs. However, on page 253 Allemann teaches that these nanospheres are for sustained release dosage forms and therefore, it would have been prima facie obvious to one of ordinary skill in the art to use Allemann's nanosphere dispersions for the water insoluble drugs with a reasonable expectation of success.

As pointed out in the earlier action, Kawata et al disclose fine powders of active agents of low solubility coated with various copolymers of met acrylic acid and methacrylic esters or hydroxypropylmethyl cellulose phthalates. The fine particles are mixed with additives and filled in capsules for oral delivery. The particles can be lyophilized. (Abstract, col. 2, lines 13-44, col. 5, lines 10-20, Examples and claims).

Igari teaches that drugs can be delivered orally using enteric-coated nanocapsule suspensions (col. 11, lines 59-61).

Kantor teaches that lipophilic compounds such as fish oils can be delivered orally by using enterically coated capsules. The lower limit of the capsules is 100 nm (Examples and claim 5).

One of ordinary skill in the art would be motivated to use Allemann et al's nanodispersons for the delivery of water insoluble drugs with a reasonable expectation of success since Kawata shows the feasibility of enteric delivery of water insoluble drugs using enteric formulations containing water insoluble drugs. One of ordinary skill in the art would be motivated to use the formulations of Allemann and containing water insoluble drugs orally since Igari and Kantor teach that suspensions of enterically coated nanocapsules can be administered orally.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Allemann fails to disclose a preparation that incorporates an active agent and that a careful reading of page 233 is required. According to applicant, Allemann specifically refers to an injectable sustained release

dosage form and that an injection is different from an oral dosage form. This argument is not persuasive. First of all, the examiner pointed out page 253 and not page 233. Secondly, instant claims are composition claims and intended use has no patentable significance and there is nothing in the reference, which precludes the administration of the nanospheres by oral administration. The very fact that one of the polymers taught by Allemann is Eudragit S is an enteric polymers implies that one can use the formulation by means other than injection since this polymer dissolves at pH 7 and upwards which is intestinal pH. The arguments by applicant that the preparations in Allemann would be suitable as a parenteral composition if poly (dl-lactic) acid were also included and that the pharmaceutical compositions of the present invention do not necessarily require the use of poly (dl-lactic acid), thus, distinguishing them is rather confusing since just as in instant composition, Allemann's composition also lacks this compound. Applicant's arguments that assuming arguendo that Allemann discloses an active agent, nowhere in Allemann is a poorly water-soluble active agent disclosed. This argument is not persuasive since Allemann's compositions are for drug delivery, which implies any drug whether it is a water-soluble drug or water insoluble drug. Applicant points out Morella in support, which according to applicant discloses a highly water-soluble active in a sustained release formulation. This argument is not persuasive since the rejection is made on Allemann's reference and not on Morella's reference.

Applicant argues that Kawata teaches a four component sustained release composition that contains a medical material, polyethylene oxide, a 1st component and a 2nd component and this composition exists as a fine powder with no aqueous

formulation base. Furthermore according to applicant, there is no suggestion or motivation to combine Allemann with Kawata since the former is a nanosuspension dispersed in an aqueous formulation base whereas the latter concerns a solid pharmaceutical dosage form. These arguments are not persuasive. First of all, instant claim language 'comprising' does not exclude the other components taught by Kawata. Secondly, Kawata is combined for its teachings of enteric delivery of the water insoluble drugs and the principle of enteric delivery of a drug, that is, delivery to the intestines, will be the same whether the formulation is in a suspension form or a solid form.

The reference of Shaw (5,318,781) is cited of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK